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EXAMINER
KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
1614	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/082,801	Applicant(s) VILLAR ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants election without traverse the Group I, claims 1-9, is acknowledged. Claims 10-11 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Claims 1-9 are currently pending for prosecution on the merits.

Information Disclosure Statement

2. Enclosed is an initialed copy of PTO 1449 which has been considered for your records, Application No. 10/082,301.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific autoimmune disease or hyperplastic disease such as lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and gliomas, but does not reasonably provide enablement for autoimmune disease or hyperplastic disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention relates to a method of treating an autoimmune or hyperplastic disease comprising administering a compound of the formula.

The instant specification defines that "treating" or "treatment" means "preventing the disease from occurring in a mammal which may be predisposed to the disease but does not yet experience or display symptoms of the disease or inhibiting the disease, i.e., arresting its development (page 5, lines 17-20).

(2) The state of the prior art

The compounds of the inventions are acridine derivatives represented by the formula. The prior art recognizes the therapeutic utility of said acridine derivatives as antihypertensives, potassium channel blockers, antiviral agents, monomeric units for dendrimers and potential anticancer and antitumor agents. However, the prior art does not recognizes cure or the

prophylactic utility of the claimed compounds in preventing disease from occurring in a mammal or complete inhibition or elimination of the disease conditions.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high, and no examples exist for efficacy of a single product against vast number of possible conditions or disease generally described as autoimmune or hyperplastic disease. Furthemore, the lack of significant guidance from the specification or prior art with regard to completely inhibiting or preventing autoimmune or hyperplastic disease with the administration of the instant composition makes practicing the claimed invention unpredictable in terms of the prevention of the disease.

(5) The breadth of the claims

The claims are very broad due to the vast number of possible diseases that can be characterized by autoimmune disease or hyperplastic disease.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA

viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of the compounds of the formula to be effective in treating the entire scope of autoimmune disease or hyperplastic disease is insufficient for enablement. The specification provides no guidance, in the way of enablement for an autoimmune or hyperplastic disease other than lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and gliomas. Furthermore, the specification provides no guidance, in the way of enablement for preventing said autoimmune or hyperplastic diseases.

(7) The presence or absence of working examples

As stated above, the specification discloses acridine derivatives represented by the formula that are used to treat autoimmune or hyperplastic diseases associated with FAS-mediated apoptosis, namely lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinomas, breast carcinomas, prostate cancers, neuroblastomas and glioma.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation

should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the activity of the compounds in treating or preventing all of disease conditions that are characterized by autoimmune or hyperplstic diseases that would be enabled in this specification.

The instant claims read on all autoimmune or hyperplastic diseases that may or may not be related to FAST-mediated apoptosis, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

For examination purposes, the phrase "treating" is interpreted as "relieving symptoms of the disease", "reducing the effects of the disease" or "causing regression of the disease".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 relates to a method of treating an autoimmune or hyperplastic diseases comprising administering the claimed compounds represented by the formula in combination with "an additional form of therapy for said disease state". It is not clear what is "an additional

form of therapy for said disease state" meant? Does it refer to known conventional form of therapy for autoimmune or hyperplastic disease? Applicant is requested to clarify.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Radzikowski et al. (Archivum Immunologiae et Therapiae Experimentalis, 1969, 17(1), 86-88).

Radzikowski teaches the use of the claimed acridine derivatives represented by the formula (e.g., 9-(dimethylaminopropylamino)-4-methoxyacridine and 9-(di-methylaminopropylamino)-2-methylacridine) for the treatment of hyperplstic disease such as tumor or cancer in mice (i.e., sarcoma and lymphoma), see Table 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radzikowski et al. (Archivum Immunologiae et Therapiae Experimentalis, 1969, 17(1), 86-88).

The teaching of Radzikoswki has been discussed in above 35 USC 102(b) rejection.

The teaching of Radzikowski differs from the claimed invention (i) in the use of 9-[(3-diethylaminopropyl)amino]acridine and (ii)the combination of other known therapy. The claims differ from the prior art by having ethyl substituent in R4 and R5 position. One having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of ethyl substituent for methyl in R4 and R5 position would not significantly

alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to use of "an additional form of therapy", the examiner determines that the addition of known therapy for the treatment of hyperplastic disease to the compounds of the formula which has been known for the treatment of cancer or tumor are well considered within the skill of the artisan. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petri et al. (Acta Microbiologica Hungarica, 1995, 42 (2), 203-8 in view of Armistead et al. (US 5192773).

Petri teaches the use of the claimed acridine derivatives represented by the formula as an immunomodulating or immunosuppressive agent (abstract; Table 1).

Armistead discloses the use of immunosuppressive compounds for the treatment of autoimmune disorders.

The teaching of Petri differs from the claimed invention in the use of said compounds for the treatment of autoimmune disease. To incorporate such teaching into the teaching of Petri, would have been obvious in view of Armistead who discloses routine knowledge in the art to utilize immunosuppressive agent in treating autoimmune disorders.

One having ordinary skill in the art would have been motivated to administer the claimed acridine derivatives having immunosuppressive property, with the reasonable expectation of

success, to a mammal to treat autoimmune disorders. One having ordinary skill in the art would have been motivated to make such modification to extend the usage of the claimed acridine derivatives in the treatment of autoimmune disorder.

Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600